EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 4
Issue: 6
16-25
Year: 2017

COMPARATIVE FORCED DEGRADATION STUDY OF THREE DIFFERENT BRANDS OF METFORMIN HCL (500MG) REGISTERED IN SUDAN

Mohamed Elamin Awadalla[1]*, Dhia Eldin Abd Elmagied Elhag[2], Abutalib Alamin Abdallah[3], Alaa E. Elawni[3], Mohammed Abdeen[4] and Hafiz Abdalrahman Mustafa[1]

[1]*Faculty of Pharmacy, University of Medical Sciences and Technology, Khartoum, Sudan.
[2]Associate Professor of Pharmaceutical Chemistry, Department of Pharmaceutical Chemistry, University of Medical Sciences and Technology, Khartoum, Sudan.
[3]Research and Development Department, Azal Pharmaceutical Industries Co. Ltd., Khartoum, Sudan.
[4]Research and Development Department, Pharmaland Pharmaceuticals Co. Ltd.

***Corresponding Author: Mohamed Elamin Awadalla**
Faculty of Pharmacy, University of Medical Sciences and Technology, Khartoum, Sudan.

Article Received on 22/03/2017 **Article Revised on 12/04/2017** **Article Accepted on 02/05/2017**

ABSTRACT
The aim of this study is to assess the stability of metformin HCl oral tablets (500 mg) upon subjecting to different acceleration stress conditions. This was achieved by determining the effect of temperature, UV light and humidity. Three brands registered in Sudan were subjected to the study, namely, Glucophage®, Formit® and Azaformin®. Glucophage® showed a sign of slight photo and thermal degradation and also showed a slight effect on the dissolution content after exposure to heat and humidity. The dissolution content of the three brands showed signs of slight effect by photolysis and also showed a decrease in potency.

KEYWORDS: Forced degradation, photolysis, thermal degradation, stability, metformin.

1. INTRODUCTION

Drug stability is the ability of a drug substance or drug product to retain its chemical, physical, microbiological and biological properties within specified limits throughout its shelf life. Stability testing is performed to determine quality of drug substance and drug product, shelf life and recommended storage conditions.

Chemical, biological and physical degradation of drug substances may change their pharmacological effects, resulting in altered efficacy therapeutic as well as toxicological consequences. Because pharmaceuticals are used therapeutically based on their efficacy and safety, they should be stable and maintain their quality until the time of usage or until their expiration date. The quality should be maintained under the various conditions that pharmaceuticals encounter, during production, storage and transportation. Therefore, understanding the factors that alter the stability of pharmaceuticals and identifying ways to guarantee their stability are critical.[1] The design of the stability studies for the finished pharmaceutical product (FPP) should be based on knowledge of the behaviour and properties of the API, information from stability studies on the API and on experience gained from studies and investigational FPPs.

All medicinal products are degraded with time. Possible degradation pathways include hydrolysis, (acid and/or base), dehydration, isomerization and racemization, elimination, oxidation, photo degradation and complex interactions with excipients and other drugs. It would be very useful if we could predict the chemical instability of a drug based on its molecular structure.[2]

Metformin HCl is an anti-diabetic drug from the biguanide class of oral antihyperglycemic agents, and used as the first line agent for the treatment of non-insulin-dependent diabetes mellitus (Type II) particularly in obese patients. Metformin HCl decreases blood glucose levels by decreasing hepatic glucose production, decreasing intestinal absorption of glucose and improving insulin sensitivity by increasing peripheral glucose uptake and utilization.[3]

2. MATERIALS AND METHODS

2.1. Materials

2.1.1. Chemicals and Reagents

The chemicals and reagents used in this study with their origins were listed below:

- Metformin HCl reference standard (potency 99.9%, water content 0.24%), Hetero Drugs Limited, India.
- Purified water.
- Potassium di-hydrogen phosphate, Duksan, Korea.
- Sodium hydroxide, Scharlau, Spain.
- Phosphoric acid, Scharlau, Spain.

All chemical and reagent mentioned above have been purchased from pharmaceuticals companies in Khartoum.

2.2. Samples

Three different brands of metformin HCl 500 mg tablets purchased from community pharmacies in Khartoum state. Their details were given below in Table 1.

Table 1: Details of metformin HCl different brands used in this study.

Trade name	Manufacturer	B.No	Mf. Date	Ex. Date
Glucophage	Merck Santé/France	280995	09/14	08/2019
Formit	Spimaco/Saudi Arabia	82672	01/15	01/18
Azaformin	Azal Pharmaceutical Industries Co.Ltd/ Sudan	07411	09/14	09/16

2.3. Instruments

- UV/vis Spectrophotometer, model 1800 240v, Shimadzu Corporation, Japan.
- pH meter and conductivity meter, model: PP20, Sartorius, Germany.
- Analytical balance, model: ED2245, Sartorius, Germany.
- Water purification system, model: NW10UV, Heal force, China.
- Mechanical shaker, model C5003, Sicherungeu, Germany.
- Ultrasonic, model WUC-A10H, Wise clean, Korea.
- Microprocessors tablets dissolution apparatus, model EL20, EI, India.
- Volumetric pipettes, volumetric flasks, mortar and pestle.

2.4. Method

The analysis was conducted according to the official United States Pharmacopoeia (USP 37) method; Ultra violet spectrophotometer, wavelength of maximum absorbance at about 233 nm, cell path length 1 cm ,water and the dissolution parameter, apparatus 1 (basket), volume 1000 ml, 100 rpm for 45 min.[4]

Metformin HCl tablets were distributed into three groups according to their brand name and subjected to same accelerated stress conditions represented by thermal with humidity at 40°C ± 2°C/75% RH ± 5% RH in stability acceleration chamber for one month and photolysis of direct sunlight for 72 hour. The assay and dissolution single point were conducted at time zero and after the tablets were subjected to the stress conditions, they were analysed.

2.5. Preparations[4]

2.5.1. Preparation of metformin HCl reference Standard for detection of λ_{max} and absorbance

About 100 mg of metformin HCl reference standard was weighed and transferred to a 100 ml V.F. then 70 ml water was added and shaken by mechanical shaker for 15 min, diluted with water to volume, 10 ml of the filtrate was diluted with water to 100 ml, another 10 ml of the resulting solution was diluted with water to 100 ml to obtain the final concentration of 0.01 mg/ml of metformin HCl reference standard.

2.5.2. Preparation of metformin HCl sample for assay

20 tablets were accurately weighed and finely powdered. An accurately weighed portion of the powder, equivalent to about 100 mg of metformin HCl was transferred to a 100 ml V.F. 70 ml water was added, then shaken by mechanical shaker for 15 min and diluted with water to volume, filtered with filter paper (Whattman), the first 20 ml of the filtrate was discarded. 10 ml of the filtrate was diluted with water to 100 ml, another 10 ml of the resulting solution was diluted with water to 100 ml to obtain the final concentration of 0.01 mg/ml of metformin HCl sample.

2.5.3. Preparation of dissolution medium

About 27.22 gm of monobasic potassium phosphate was weighed and dissolved in water, diluted with water to 1000 ml. About 8.0 gm of sodium hydroxide were dissolved in water, then diluted with water to 1000 ml to obtain 0.2 M NaOH. 50 ml of the monobasic potassium phosphate solution were placed in a 200 ml volumetric flask, and about 22.4 ml of sodium hydroxide were added, finally the solution was made up with water to volume.

2.5.4. Preparation of Standard for dissolution

About 50 mg from metformin reference standard was weighed and put in 100 ml of the dissolution medium, 2 ml was taken and transferred in 100 ml V.F, then completed to volume by the dissolution medium to obtain the final concentration of 0.01 mg/ml.

2.5.5. Preparation of sample for dissolution

Six tablets were accurately weighed and put into the basket. After 45 minutes, sample was filtered through Whattman filter paper, about 2 ml from these solutions were taken and transferred to 100 ml V.F, then completed to volume by the dissolution medium.

2.5.6. Preparation of sample for photo degradation

Sixty tablets of Glucophage, Formit and Azaformin were exposed to direct sunlight for 72 hrs. The maximum temperature at 12 pm within three days was 42°C, 40°C and 43°C, respectively. 20 of them were used to carry out the assay of the product and 6 of them used to run the dissolution test according to the method.

2.5.7. Preparation of sample for thermal degradation

Sixty tablets of Glucophage, Formit and Azaformin were put in accelerated condition chamber, 40°C/RH 75% for one month. 20 of them were used to carry out the assay of the product, 6 of them used to run the dissolution test according to the method.

3. RESULTS AND DISCUSSION

The following formula was used to calculate content percentage of metformin HCl.

$$Q\% = \frac{At}{As} x \frac{Cs}{Ct} x \frac{P}{100} x \frac{(100 - Wc)}{100} x 100$$

Which:

At = absorbance from the Sample solution
As = absorbance from the Standard solution
Cs = concentration of Standard solution (mg/mL)
Ct = concentration of the Sample solution (mg/mL)
P = potency of RS
Wc = water content of RS

3.1. Absorbance spectrum of metformin HCL standard

Scanning of λ_{max} of metformin HCl standard:

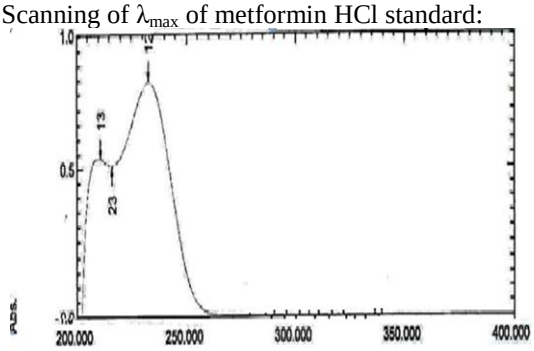

Figure 1: Chromatogram of metformin HCl reference standard which gave strong absorbance peak at 233 nm.

3.2. Stability test of Glucophage tablets

The average absorbance and concentration of standard were 0.802 nm and 0.01002 mg/ml, respectively.

3.2.1. Sample at time zero

3.2.1.1. Assay of Glucophage

The analysis was carried out to calculate the average absorbance and concentration for the two samples before subjecting to stress factors as described in the method and the results obtained were 0.798 nm, 0.009987 mg/ml for sample 1 and 0.797 nm, 0.009997 mg/ml for sample2.

$$Q1\% = \frac{0.798}{0.802} x \frac{0.01002}{0.009987} x \frac{99.9}{100} x \frac{(100 - 0.24)}{100} x 100 = 99.5\%$$

$$Q2\% = \frac{0.797}{0.802} x \frac{0.01002}{0.009997} x \frac{99.9}{100} x \frac{(100 - 0.24)}{100} x 100 = 99.3\%$$

The average content percentage of assay of Glucophage tablets at time zero was 99.4%. The result complies with USP acceptance criteria (95%-105%).

3.2.1.2. The dissolution test of Glucophage

Table 2: Average weight of tablets used for dissolution test at time zero.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	537	537.3	532.9	531.1	531.1	535.4	534.1

The average absorbance and concentration of the standard used for dissolution test of Glucophage at time zero were 0.82 nm and 0.01 mg/ml respectively.

Table 3: Average absorbance and concentration of Glucophage used for dissolution test at time zero.

Read No	1	2	3	Average	Conc mg/ml
Sample1	0.825	0.823	0.828	0.83	0.01005
Sample2	0.832	0.839	0.833	0.83	0.01005
Sample3	0.82	0.82	0.82	0.82	0.00997
Sample4	0.821	0.823	0.821	0.822	0.00994
Sample5	0.821	0.821	0.821	0.821	0.00994
Sample6	0.844	0.842	0.843	0.84	0.01002

Table 4: Content percentage of dissolution of Glucophage tablets at time zero.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	100.3%	100.3%	99.9%	100.5%	100.4%	101.8%	100.53

3.2.2. The photolysis test of Glucophage tablets

3.2.2.1. Assay of Glucophage sample after photolysis

Average absorbance and concentration of Glucophage after photolysis for the two samples were 0.81 nm, 0.010001 mg/ml and 0.809 nm, 0.009987 mg/ml respectively.

The content percentage analysis was carried out as described earlier and the results were as follows:

$$Q1\% = \frac{0.81}{0.822} x \frac{0.01001}{0.010001} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 98.3\%$$

$$Q2\% = \frac{0.809}{0.822} x \frac{0.01001}{0.0.009987} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 98.3\%$$

The average content percentage of assay of Glucophage tablets after photolysis was 98.3%. The result complies with USP acceptance criteria (95%-105%).

3.2.2.2. The dissolution test of Glucophage sample after photolysis

Table 5: Average weight of Glucophage tablets used for dissolution test after photolysis.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	536.7	538	533	537	528	535	534.6

Table 6: Average absorbance and concentration of Glucophage used for dissolution test after photolysis.

ABS No	1	2	3	Average	Conc mg/ml
Sample1	0.8	0.82	0.81	0.81	0.01004
Sample2	0.813	0.813	0.813	0.813	0.01006
Sample3	0.81	0.81	0.81	0.81	0.00997
Sample4	0.809	0.808	0.807	0.808	0.01005
Sample5	0.799	0.8	0.798	0.799	0.00988
Sample6	0.8	0.8	0.8	0.8	0.01001

Table 7: Content percentage of dissolution of Glucophage tablets after photolysis.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	99%	99.1%	99.7%	98.7%	99.3%	98.1%	99%

3.2.3. The thermal test of Glucophage tablets

3.2.3.1. Assay of Glucophage after thermal acceleration

The average absorbance and concentration of the two samples of Glucophage after thermal acceleration were 0.812 nm, 0.010006 mg/ml for sample1 and 0.812 nm, 0.009978 mg/ml for sample2.

$$Q1\% = \frac{0.812}{0.813} x \frac{0.01}{0.010006} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.5\%$$

$$Q2\% = \frac{0.812}{0.813} x \frac{0.01}{0.009978} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.8\%$$

3.2.3.2. Dissolution test of Glucophage sample after thermal acceleration

Table 8: Average weight of Glucophage used for dissolution test after thermal acceleration.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	**536**	**536**	**540**	**539**	**525**	**538**	**535.6**

Table 9: Average absorbance and concentration of Glucophage used for dissolution test after thermal acceleration.

ABS No	1	2	3	Average	Conc mg/ml
Sample1	0.815	0.815	0.815	0.815	0.010007
Sample2	0.815	0.813	0.813	0.814	0.010007
Sample3	0.13	0.82	0.82	0.812	0.010082
Sample4	0.815	0.815	0.815	0.815	0.010063
Sample5	0.814	0.814	0.813	0.814	0.009802
Sample6	0.816	0.816	0.815	0.816	0.010045

Table 10: Content percentage of dissolution of Glucophage tablets after thermal acceleration.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	99.3%	98.9%	98.2%	99.2%	101, 2%	99%	98.83%

Table 11: A summary of the Q% of Glucophage according to the tests done and applied conditions.

Test	Condition	Q%
Assay	Before subjecting to stress factors	99.4
Dissolution	Before subjecting to stress factors	100.53
Assay	After subjecting to photolysis	98.3
Dissolution	After subjecting to photolysis	99
Assay	After subjecting to thermal acceleration test	99.7
Dissolution	After subjecting to thermal acceleration test	98.83

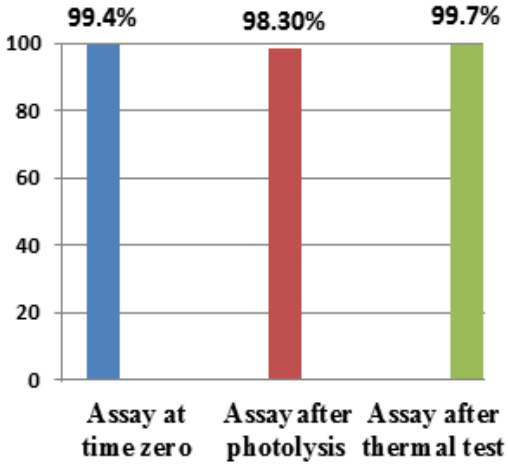

Figure 2: Content percentage of assay of Glucophage tablets.

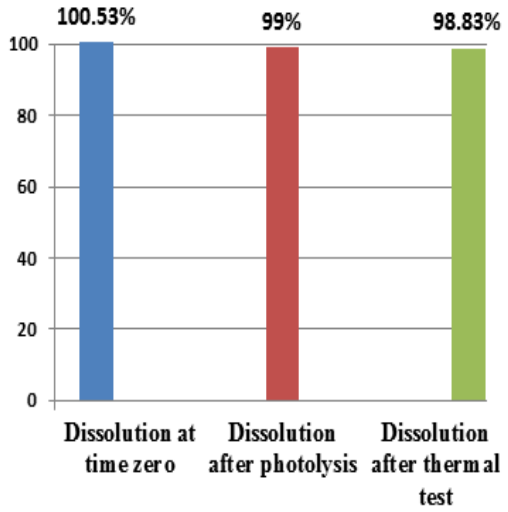

Figure 3: Content percentage of dissolution of Glucophage tablets.

3.3. Stability test of Formit tablets

3.3.1. Sample at time zero

3.3.1.1. Assay of Formit

The analysis was carried out to calculate the average absorbance and concentration for the two samples before subjecting to stress factors as described in the method and the results obtained were 0.797 nm, 0.01 mg/ml for sample1 and 0.796 nm, 0.01 mg/ml for sample2.

$$Q1\% = \frac{0.797}{0.8} x \frac{0.01002}{0.01} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.5\%$$

$$Q2\% = \frac{0.796}{0.8} x \frac{0.01002}{0.01} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.4\%$$

The average content percentage of assay of Formit tablets at time zero was 99.5%.

3.3.1.2. The dissolution test of Formit

Table 12: Average weight of Formit tablets used for dissolution test at time zero.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	559.2	665.8	655.2	660.2	654.2	666.6	660.2

Table 13: Average absorbance and concentration of Formit used for dissolution test at time zero.

Read No	1	2	3	Average	Conc mg/ml
Sample1	0.798	0.798	0.797	0.798	0.009985
Sample2	0.807	0.807	0.808	0.807	0.010085
Sample3	0.81	0.809	0.809	0.809	0.009924
Sample4	0.81	0.809	0.81	0.81	0.010000
Sample5	0.805	0.805	0.805	0.805	0.009909
Sample6	0.83	0.829	0.83	0.83	0.010097

Table 14: Content percentage of dissolution of Formit at time zero.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	99.6%	99.7%	101.6%	100.9%	101.2%	102.4%	100.9%

3.3.2. The photolysis test of Formit

3.3.2.1. Assay of Formit sample after photolysis

Average absorbance and concentration of standard were 0.835 nm and 0.01mg/ml respectively.

$$Q1\% = \frac{0.831}{0.835} x \frac{0.01}{0.010002} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.2\%$$

$$Q2\% = \frac{0.833}{0.835} x \frac{0.01}{0.009986} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.6\%$$

The average content percentage of assay of Formit after photolysis was carried out as described earlier and the result obtained was 99.4%.

3.3.2.2. The dissolution test of Formit sample after photolysis

Table 15: Average weight of the tablets used for dissolution test of Formit after photolysis.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	649.6	648.3	650.5	661.4	649.9	650.9	651.8

Table 16: Average absorbance and concentration of Formit samples used for dissolution test after photolysis.

Read No	1	2	3	Average	Conc mg/ml
Sample1	0.823	0.824	0.824	0.824	0.009966
Sample2	0.825	0.825	0.825	0.825	0.009946
Sample3	0.834	0.834	0.835	0.834	0.00998
Sample4	0.838	0.838	0.838	0.838	0.010147
Sample5	0.832	0.829	0.831	0.831	0.009971
Sample6	0.82	0.83	0.84	0.83	0.009986

Table 17: Content percentage of dissolution of Formit tablets after photolysis.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	99%	99.4%	100.1%	99%	100%	100.2%	99.61%

3.3.3. The thermal test of Formit

3.3.3.1. Assay of Formit after thermal acceleration

Average absorbance and concentration of standard were 0.8 nm and 0.01002 mg/ml respectively.

Average absorbance and concentration of Formitafter thermal acceleration for the two samples were 0.81 nm, 0.009998 mg/ml and 0.799 nm, 0.010002 mg/ml respectively.

$$Q1\% = \frac{0.81}{0.8} x \frac{0.01002}{0.009998} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 101.1\%$$

$$Q2\% = \frac{0.799}{0.8} x \frac{0.01002}{0.010002} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.7\%$$

The average content percentage of Formit after thermal acceleration was carried out as described earlier in and the results obtained were 100.4%.

3.3.3.2. The dissolution test of Formit sample after thermal acceleration

Table 18: Average weight of the tablets used for dissolution test of Formit after thermal acceleration.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	643.9	651.3	646.9	647.4	656.6	645.4	648.58

Average absorbance and concentration of the standard used for thermal acceleration were 0.836 nm and 0.01002 mg/ml respectively.

Table 19: Average absorbance and concentration of Formit samples used for dissolution test after thermal acceleration.

Read No	1	2	3	Average	Conc mg/ml
Sample1	0.774	0.774	0.774	0.774	0.009928
Sample2	0.822	0.822	0.823	0.823	0.010042
Sample3	0.795	0.795	0.795	0.795	0.009974
Sample4	0.819	0.82	0.818	0.819	0.009982
Sample5	0.788	0.788	0.788	0.788	0.010124
Sample6	0.823	0.822	0.822	0.822	0.009951

Table 20: Content percentage of dissolution of Formit after thermal acceleration.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	93.1%	97.9%	95.2%	98%	93%	98.8%	96%

Table 21: Q% of Formit tablet according to the test done and applied conditions.

Test	Condition	Q%
Assay	Before subjecting to stress factors	99.5
Dissolution	Before subjecting to stress factors	100.9
Assay	After subjecting to photolysis	99.4
Dissolution	After subjecting to photolysis	99.61
Assay	After subjecting to thermal acceleration test	100.4
Dissolution	After subjecting to thermal acceleration test	96

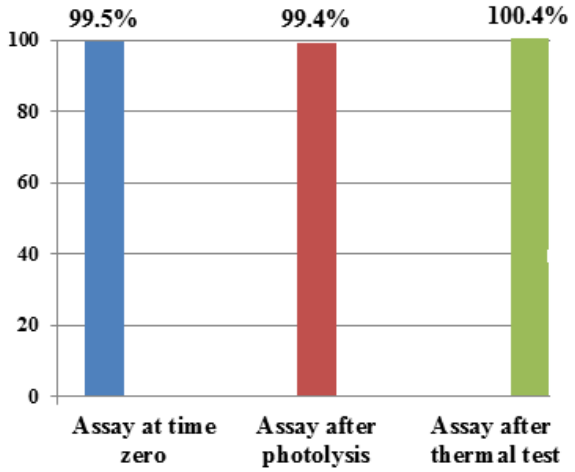

Figure 4: Content percent of assay of Formit tablets.

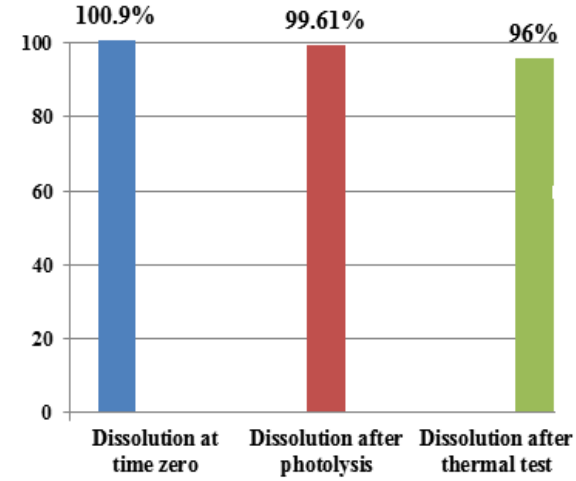

Figure 5: Content percentage of dissolution of Formit tablets.

3.4. Stability test of Azaformin tablets

The average absorbance and concentration of standard were 0.826 nm and 0.01 mg/ml respectively.

3.4.1. Sample at time zero

3.4.1.1. Assay of Azaformin

The analysis was carried out to calculate the average absorbance and concentration for the two samples before subjecting to stress factors as described in the method and the results obtained were 0.822 nm, 0.010004 mg/ml for sample1 and 0.821 nm, 0.009994 mg/ml for sample2.

$$Q1\% = \frac{0.822}{0.826} x \frac{0.01}{0.010004} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.1\%$$

$$Q2\% = \frac{0.821}{0.826} x \frac{0.01}{0.009994} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.1\%$$

The average content percentage of assay ofAzaformin tablets at time zero was 99.1%.

3.4.1.2. Dissolution test of Azaformin sample at time zero

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	535.7	625.6	529.5	529.1	530.4	529	530.2

Table 22: Average weight of the tablets used for dissolution test of Azaformin at time zero.

Average absorbance and concentration of standard were 0.826 nm and 0.01006 mg/ml respectively.

Table 23: Average absorbance and concentration of the samples used for dissolution test of Azaformin at time zero.

Read No	Conc mg/ml	1	2	3	Average
Sample1	0.010104	0.824	0.824	0.824	0.824
Sample2	0.009913	0.826	0.826	0.826	0.826
Sample3	0.009987	0.82	0.826	0.824	0.825
Sample4	0.009979	0.819	0.818	0.82	0.819
Sample5	0.010004	0.822	0.822	0.822	0.822
Sample6	0.09977	0.825	0.825	0.825	0.825

Tables 24: Content percentage of dissolution of Azaformin at time zero.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	98.4%	100.5%	99.8%	99%	99.1%	99.8%	99.4%

3.4.2. The photolysis test of Azaformin sample

3.4.2.1. Assay of Azaformin sample after photolysis

Average absorbance and concentration of standard were 0.825 nm and 0.01mg/ml respectively.

Average absorbance and concentration of Azaformin after photolysis for the two samples were 0.822 nm, 0.010004 mg/ml and 0.822 nm, 0.010003 mg/ml respectively.

$$Q1\% = \frac{0.822}{0.825} x \frac{0.01}{0.010004} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.3\%$$

$$Q2\% = \frac{0.822}{0.825} x \frac{0.01}{0.010003} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 99.3\%$$

The average content percentage of assay of Azaformin after photolysis was carried out as described earlier and the result obtained was 99.3%.

3.4.2.2. The dissolution test of Azaformin sample after photolysis

Table 25: Average weight of tablets used for dissolution test of Azaformin after photolysis.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	545.4	527.8	539.7	541.3	535.6	529.8	535.98

Average absorbance and concentration of standard used for dissolution of test of Azaformin after photolysis were 0.825 nm and 0.01 mg/ml respectively.

Table 26: Average absorbance and concentration of Azaformin used for dissolution test after photolysis.

Read No	Conc mg/ml	1	2	3	Average
Sample1	0.010176	0.811	0.811	0.811	0.81
Sample2	0.009847	0.806	0.807	0.807	0.807
Sample3	0.010069	0.809	0.81	0.808	0.809
Sample4	0.010099	0.81	0.81	0.81	0.81
Sample5	0.009993	0.806	0.808	0.707	0.807
Sample6	0.009885	0.808	0.808	0.808	0.808

Table 27: Content percentage of dissolution of Azaformin after photolysis.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	96.3%	99%	97%	96.7%	97.6%	98.8%	97.6%

3.4.3. The thermal test of Azaformin

3.4.3.1. Assay of Azaformin after thermal acceleration

Average absorbance and concentration of standard used were 0.799 nm and 0.01 mg/ml respectively.

Average absorbance and concentration of the two sample of Azaformin after thermal acceleration were 0.811 nm, 0.01 mg/ml for sample1 and 0.81 nm, 0.010009 mg/ml for sample2.

$$Q1\% = \frac{0.811}{0.799} x \frac{0.01}{0.01} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 101.2\%$$

$$Q2\% = \frac{0.81}{0.799} x \frac{0.01}{0.010009} x \frac{99.9}{100} x \frac{(100-0.24)}{100} x100 = 100.9\%$$

The average content percentage of Azaformin after thermal acceleration was carried out as described earlier in and the results obtained were 101%.

3.4.3.2. The dissolution test of Azaformin sample after thermal acceleration

Table 28: Average weight of the tablets used for dissolution test of Azaformin after thermal acceleration.

Tablet No	1	2	3	4	5	6	AVG
Wt/mg	539.3	526.5	532.6	541.7	519.6	527.8	531.25

Average absorbance and concentration of the standard used for dissolution test of Azaformin after thermal acceleratin were 0.797 nm and 0.01002 mg/ml respectively.

Table 29: Average absorbance and concentration of the samples used for dissolution test of Azaformin after thermal acceleration.

Read No	Conc mg/ml	1	2	3	Average
Sample1	0.010152	0.797	0.799	0.798	0.798
Sample2	0.009911	0.799	0.799	0.799	0.799
Sample3	0.010025	0.799	0.798	0.799	0.799
Sample4	0.010197	0.826	0.826	0.825	0.826
Sample5	0.009781	0.827	0.827	0.828	0.827
Sample6	0.009935	0.782	0.781	0.782	0.782

Table 30: Content percentage of dissolution of Azaformin after thermal acceleration.

	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6	Average
Q%	98.1%	101.1%	99.9%	101.5%	105.9%	98.6%	100.9 %

Table 31: Q% of Azaformin according to the tests done and applied conditions.

Test	Condition	Q%
Assay	Before subjecting to stress factors	99.1
Dissolution	Before subjecting to stress factors	99.4
Assay	After subjecting to photolysis	99.4
Dissolution	After subjecting to photolysis	97.6
Assay	After subjecting to thermal acceleration test	101.1
Dissolution	After subjecting to thermal acceleration test	100.76

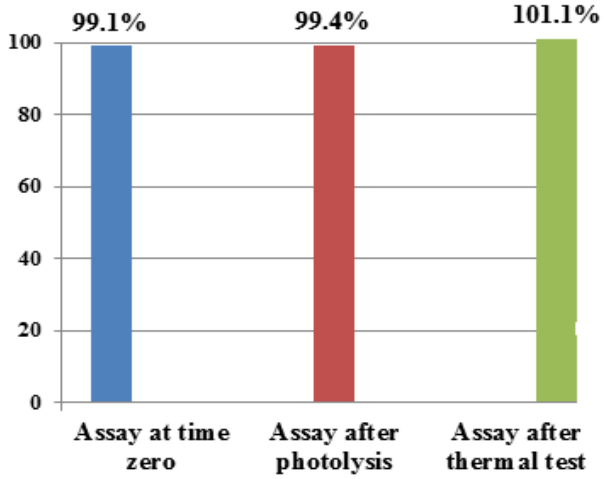

Figure 6: Content percentage of assay of Azaformin tablets.

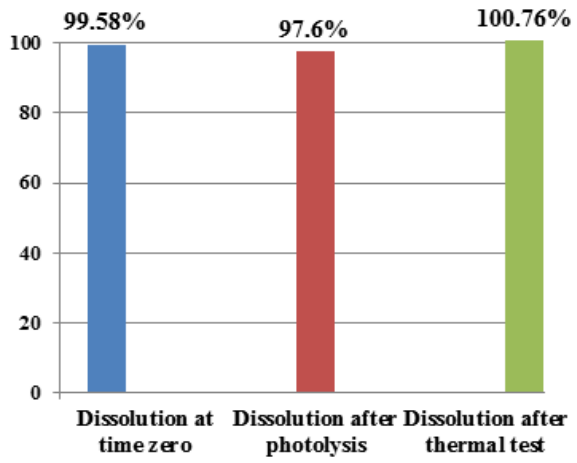

Figure 4.7: Content percentage of dissolution of Azaformin tablets.

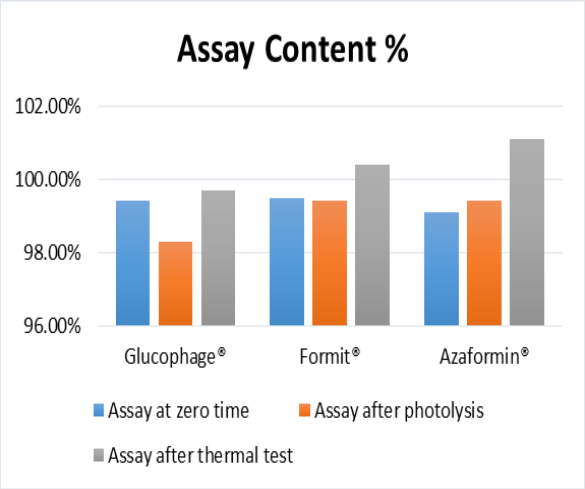

Figure 8: Content% of the assay of the 3 brands.

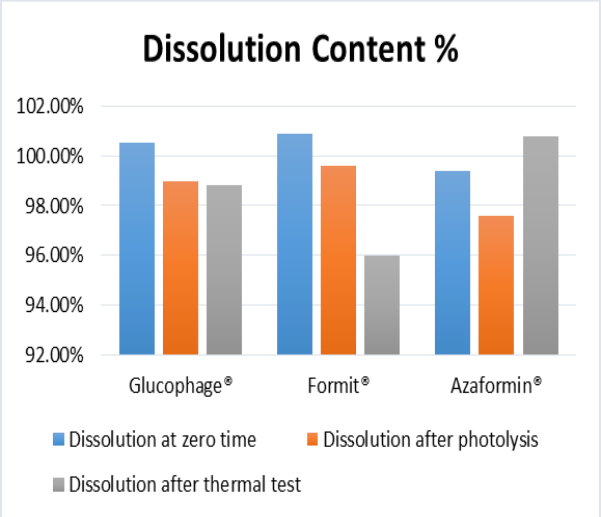

Figure 9: Content% of the dissolution of the 3 brands.

4. CONCLUSION AND RECOMMENDATIONS

4.1. Conclusion

From the results obtained in this study, the following conclusions could be drawn:

- All brands of metformin results were within the stated limit for assay before applying any degradation stress conditions.
- All brands of metformin results were within the stated limit for dissolution before applying any degradation stress conditions.
- Only Glucophage was showing a sign of slight degradation by photolysis.
- Only Glucophage was showing a sign of slight degradation by heat and humidity.
- The dissolution content of Glucophage, Formit and Azaformin showed a signs of slight effect by photolysis and also showed a decrease in potency. This may be due to the effect of photolysis on the dissolution and/or release of the drug.
- Only the dissolution content of Glucophage showed signs of slight effect by heat and humidity.
- Formit and Azaformin showed some deviation within their dissolution results of the samples. This may be related to the weight uniformity or to a technical error.

4.2. Recommendations

According to the results and findings of the present study, the following is recommended:

- Patient should be given restricted advices on correct storage conditions for any dispensed drugs.
- Metformin HCl must be packaged in a well closed containers and always protected from light and humidity.
- Coating tablets with polymer film will help in the protection of the tablet.
- More studies must be done to evaluate the effect of light, heat and humidity on the dissolution and release of metformin.
- In-depth study to metformin HCl tablets and its degradation by light, heat and humidity must be conducted.

5. REFERENCES

1. Yoshioka Stella V. Stability of drugs and dosage forms. 1st ed. New York: Kluwer Academic; 2004.
2. Tønnesen H. Photostability of drugs and drug formulations. 1st ed. Boca Raton [etc.]: CRC Press; 2004.
3. Viollet B, Guigas B, Garcia N, Leclerc J, Foretz M, Andreelli F. Cellular and molecular mechanisms of metformin: an overview. Clinical Science. 2012; 122(6): 253-270.
4. The United States Pharmacopeia 2014: USP 37; The national formulary: NF 32. Rockville, MD: United States Pharmacopeial Convention; 2014.